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ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Md Moshiur Rahman, MBBS, Assistant Professor, Department of Neurosurgery, Holy Family Red Crescent Medical College Hospital, Dhaka 1000, Bangladesh. dr.tutul@yahoo.com

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The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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CASE REPORT

Multifocal papillary thyroid cancer in Graves' disease: A case report

Naweed Alzaman

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Naweed Alzaman, Department of Internal Medicine, Taibah University College of Medicine, Tayba 42353, Al-Madinah al-Munawwarah, Saudi Arabia

Corresponding author: Naweed Alzaman, MD, Assistant Professor, Department of Internal Medicine, Taibah University College of Medicine, Janadah Bin Umayyah Road, Tayba 42353, Al-Madinah al-Munawwarah, Saudi Arabia. nzaman@taibahu.edu.sa

Abstract

BACKGROUND

Thyroid cancer is not commonly observed in patients with Graves' disease (GD). The presence of thyroid nodules in GD is not uncommon. However, a link between these two entities has been reported. Herein, we report the case of a patient with GD and thyroid cancer in Saudi Arabia, which has not been reported previously in our region.

CASE SUMMARY

A 26-year-old male patient with GD, receiving carbimazole for 2 years, presented to our hospital. His hyperthyroidism was controlled clinically and biochemically. On clinical examination, he was found to have a left-sided thyroid nodule. Ultrasound revealed a 2.6 cm hypoechoic nodule with high vascularity. He was then referred for fine needle aspiration which showed that the nodule was highly suspicious for malignancy. The patient underwent total thyroidectomy and was diagnosed with multifocal classical micropapillary thyroid cancer. Post thyroidectomy he received radioactive iodine ablation along with levothyroxine replacement therapy.

CONCLUSION

Careful preoperative assessment and thyroid gland ultrasound might assist in screening and diagnosing thyroid cancer in patients with GD.

Key Words: Graves' disease; Thyroid cancer; Thyroid nodules; Ultrasound; Multifocal; Case report

Core Tip: Thyroid cancer in male patients with Graves' disease (GD) is rare. We report the first case of multifocal micropapillary thyroid cancer in a young male patient with GD in Saudi Arabia, which was detected by careful clinical examination followed by ultrasonographic evaluation of the nodule.

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INTRODUCTION

Thyroid-stimulating immunoglobulins (TSI) induce thyroid hormone overproduction in Graves' disease (GD), the most common cause of hyperthyroidism. While GD is not generally considered a risk factor for developing thyroid cancer, which ranks as the eighth most prevalent cancer worldwide[1], other risk factors include childhood exposure to ionizing radiation and iodine deficiency[2].

Thyroid carcinoma in GD was initially regarded as an infrequent phenomenon. However, the prevalence of thyroid carcinoma in patients with GD has recently increased compared with that in the normal population[2,3].

The occurrence of thyroid nodules in patients with GD varies between 13% and 37%[4]. Some evidence suggests that individuals with autoimmune thyroid conditions face a higher risk of thyroid cancer due to elevated expression of biomarkers associated with oxidative DNA damage[1]. Additionally, it has been suggested that TSI can stimulate growth and promote angiogenesis by activating growth factor pathways[3].

The prevalence of thyroid cancer among patients with GD in Saudi Arabia remains unknown. We report a case of multifocal papillary thyroid cancer in a young male who has been undergoing treatment for hyperthyroidism over the past 2 years.

CASE PRESENTATION

Chief complaints

Neck swelling.

History of present illness

A 26-year-old male patient was diagnosed with GD two years ago and had been undergoing treatment with carbimazole.

History of past illness

Initially, he was on a regimen of carbimazole 45 mg for one year. However, a few months before his current presentation, his dose was gradually reduced to 20 mg.

Personal and family history

The patient denied any family history of malignant tumors.

Physical examination

During his recent clinical assessment, physical examination revealed an enlarged goiter and the presence of a palpable nodule in the left thyroid lobe. Concerns were raised about the progression of his GD and the development of this thyroid nodule.

Laboratory examinations

Laboratory investigations yielded notable results: His thyroid-stimulating hormone (TSH) level was 0.27, while the free T4 level was 0.99. A significant elevation in TSI was also observed, measuring 4.91 IU/L (normal range < 1.7 IU/L).

Imaging examinations

Further evaluation by thyroid ultrasound unveiled a distinct hypoechoic nodule located in the left thyroid lobe. This nodule measured 2.4 cm × 2.2 cm × 2.6 cm, displaying a smooth border and increased vascularity (Figure 1). The nodule was classified as TIRADS 4, indicating a high level of suspicion. To gain deeper insights, a nuclear scan utilizing technetium 99m pertechnetate was conducted. The results revealed a heightened homogeneous thyroid uptake of 59%. Notably, dominant cold nodules were identified in the left thyroid lobe through this scan (Figure 2).

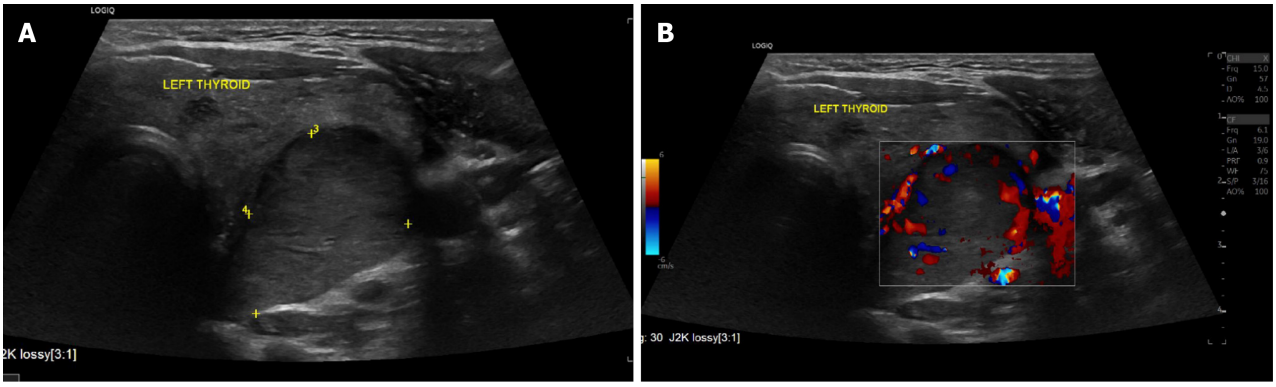

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Figure 1 Thyroid ultrasound. A: Left sided thyroid nodule oval shaped; B: With increased vascularity.

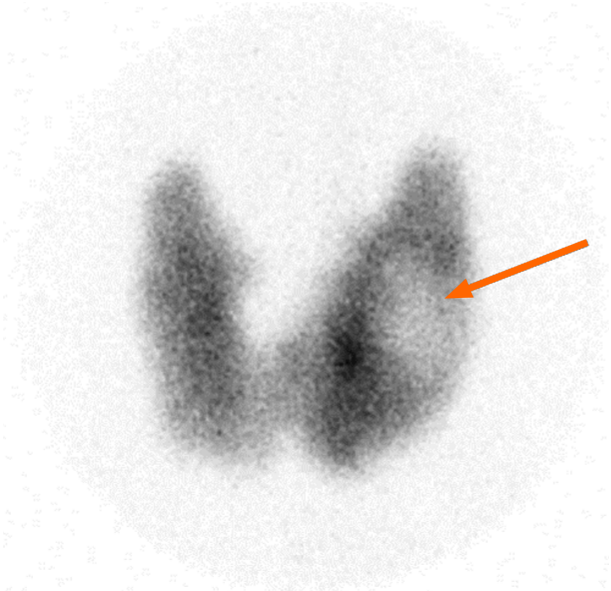

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Figure 2 Technetium scan (Tc-99m) showing hyperthyroid gland with cold nodule (the arrow points to a cold nodule in the left thyroid lobe).

MULTIDISCIPLINARY EXPERT CONSULTATION

Fine needle aspiration cytology analysis was performed to characterize the nodule further. Clusters, papillae, and sheets of cells were observed, and their overlapping nuclear grooves hinted at features suggestive of papillary thyroid carcinoma. The nodule was therefore classified as Bethesda Category 4[5].

FINAL DIAGNOSIS

Multifocal classical papillary microcarcinoma in both thyroid lobes.

TREATMENT

In light of these findings, a decision was made for the patient to undergo total thyroidectomy with lymph node dissection. The pathological evaluation following the procedure indicated multifocal classical papillary microcarcinoma in both thyroid lobes (Figure 3). The largest nodule measured 0.8 cm in diameter and displayed focal lymphatic invasion. However, three right paratracheal lymph nodes were confirmed to be negative for carcinoma.

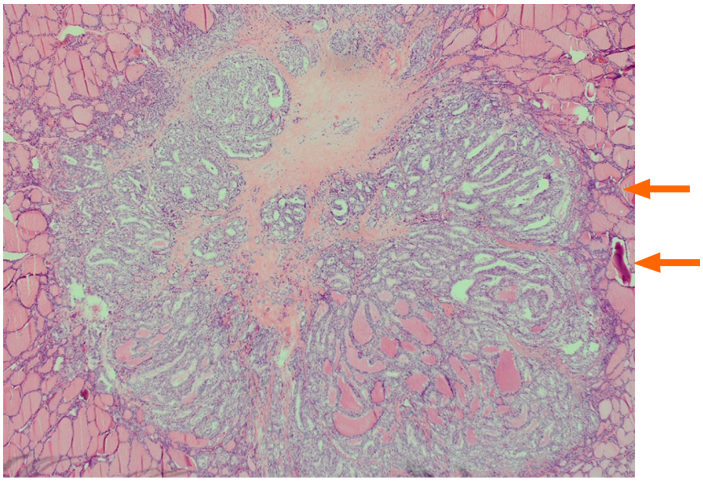

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Figure 3 Papillary thyroid cancer showing neoplastic papillae (upper arrow) and psammoma bodies (lower arrow).

OUTCOME AND FOLLOW-UP

Following the surgery, the patient received radioactive iodine ablation therapy, with a dose of 102.53 mCi of radioactive Iodine-131. This multifaceted approach aimed to address both GD and the identified papillary thyroid carcinoma.

DISCUSSION

Historically, hyperthyroidism was considered protective against thyroid cancer due to suppressed TSH levels. Consequently, thyroid cancer was often excluded as a concern in patients with GD[6,7]. However, recent studies have challenged this perspective by revealing instances of concurrent thyroid cancer and hyperthyroidism. The investigation into the coexistence of these diseases, including GD, toxic multinodular goiter (TMNG), and Hashimoto's disease, has become a subject of interest[8,9]. Nevertheless, it is important to approach the findings of such studies with caution due to their retrospective nature, which can introduce selection and recall bias.

The American Thyroid Association recommends fine needle aspiration for nonfunctioning or hypofunctioning nodules identified through nuclear scans in patients with hyperthyroidism, as these nodules carry a higher risk of malignancy. Surgical intervention is advised for cases with suspicious or diagnostic cytopathology results[10].

Recent meta-analyses have revealed that the prevalence of thyroid carcinoma in GD is higher than global figures, with 10%-15% of GD-associated nodules reported to be thyroid cancers, predominantly papillary thyroid cancer[3]. This case report presents a young male with GD and a highly suspicious thyroid nodule. The results of fine needle aspiration biopsy were highly suggestive of papillary thyroid cancer. In addition, clinical examination and ultrasound were instrumental in identifying the nodule, and after total thyroidectomy, we established a definitive diagnosis of multifocal papillary microcarcinoma. Patients with multifocal papillary thyroid cancer have higher postoperative disease progression than those with unifocal papillary thyroid cancer patients[11].

Notably, research from the University of Chicago indicated that among patients with GD who underwent total thyroidectomy, 20% were diagnosed with both GD and thyroid cancer. These cases were primarily middle-aged females with positive TSI, and most of them presented with unifocal microcarcinomas[12]. Local data at Saudi Arabia showed that majority of patients with GD underwent total thyroidectomy because of failed antithyroid drugs and severe ophthalmopathy[13], while a retrospective study in Saudi Arabia demonstrated that only 5% of patients with thyroid cancer undergoing thyroidectomies were identified as hyperthyroid, with limited details regarding cancer characteristics[14].

The prognosis of thyroid cancer in patients with GD remains a topic of debate. While some studies suggest more aggressive behavior and higher recurrence rates[15,16], others find no significant differences in outcomes[17,18]. Moreover, conflicting findings exist, with certain studies reporting better prognosis and longer disease-free survival[19].

Recent umbrella reviews have incorporated both prospective and retrospective studies, revealing varying evidence regarding the risk of thyroid cancer in patients with GD. These reviews suggest a modest risk compared to patients with TMNG, while a stronger risk is observed in patients with GD with nodules compared to those without. Risk appears modest in patients with GD with solitary nodules compared to those with multiple nodules. In terms of recurrence, persistence, and prognosis, moderate evidence exists for patients with hyperthyroidism regardless of GD, but no clear evidence supports a higher risk in patients with GD compared to those with euthyroidism[20].

Thyroid cancer might not be promptly recognized in the context of GD. This case report underscores the importance of preoperative assessment, involving ultrasound, nuclear imaging, and fine needle aspiration, if necessary, to stratify cancer risk. Routine ultrasound is not typically recommended for GD evaluation, as a clinical presentation with suppressed TSH and elevated TSI is often deemed sufficient. Nonetheless, the coexistence of GD and thyroid cancer, albeit uncommon, underscores the necessity of vigilant evaluation, particularly in the presence of thyroid nodules.

CONCLUSION

This case sheds light on the evolving understanding of the coexistence of GD and thyroid cancer. The intricate relationship between these conditions challenges historical assumptions and emphasizes the need for careful evaluation in patients with GD with thyroid nodules. Based on this case, it is recommended to incorporate ultrasound and nuclear imaging, along with fine needle aspiration when appropriate, to assess malignancy risk. Clinicians should consider these measures for patients with GD and thyroid nodules to ensure timely detection and tailored management strategies. Further research could delve into the prevalence of thyroid cancer among patients with GD and explore the impact of various interventions on patient outcomes. Incorporating these insights into clinical practice will enable improved care for this unique subset of patients

FOOTNOTES

Author contributions: Alzaman N confirms sole responsibility for the following: study conception and design, data collection, analysis, interpretation of results and manuscript preparation.

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Country/Territory of origin: Saudi Arabia

ORCID number: Naweed Alzaman 0000-0002-1543-1132.

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